General

Guideline Title

Risk reduction and surveillance strategies for individuals at high genetic risk for breast and ovarian cancer.

Bibliographic Source(s)

Alberta Provincial Breast Tumour Team. Risk reduction and surveillance strategies for individuals at high genetic risk for breast and ovarian cancer. Edmonton (Alberta): Alberta Health Services, Cancer Care; 2011 Apr. 14 p. (Clinical practice guideline; no. BR-011). [47 references]

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Breast Cancer Risk Reduction and Surveillance

1. Surgery: Prophylactic Bilateral Mastectomy
    - Benefits and risks of prophylactic bilateral mastectomy should be raised for *BRCA1* and *BRCA2* mutation carriers but can also be discussed on a case-by-case basis for other women in the target population.
    - The possibility of an incidental breast cancer being diagnosed, and breast reconstruction options should be discussed in advance.
    - Prophylactic bilateral mastectomy should be performed by a breast surgeon. Preservation of the nipple and areola could be considered; however the patient should be informed that there is currently little evidence on this topic and that there is a slightly increased risk of breast cancer (versus complete removal of nipple and areola) and possible loss of sensation and ischemia.
    - Excised tissue should be examined by a pathologist who is aware of the individual's high genetic risk status, and who is experienced in breast cancer pathology.
    - Mammography and magnetic resonance imaging (MRI) should not be part of routine surveillance practice after bilateral mastectomy or reconstruction.

    Prior to, or in the absence of, bilateral prophylactic mastectomy, surveillance and other risk reduction options can be considered.

2. Recommended Screening for Those with Intact Breasts
    - Both mammography and MRI should be offered on an annual basis from age 25-30 years to age 65-69 years.
        - Individuals should be informed of the potential for false negative results (leading to a breast cancer diagnosis between screening rounds) and false positive results (leading to recall imaging studies and possibly unnecessary biopsies) associated with this approach.

        - In addition, individuals and their physicians should be aware that MRI should be requested at least six months prior to the desired screening date.
    - Where available, MRI should be performed at a centre with a dedicated breast coil and experienced breast radiologists. Full recommendations for the use of MRI in patients with breast cancer were developed by Alberta Health Services, Cancer Care in 2010 (see the National Guideline Clearinghouse [NGC] summary of the Alberta Health Services, Cancer Care guideline Magnetic Resonance Imaging for Breast Cancer Screening, Pre-operative Assessment, and Follow-up).
    - For annual breast screening, the addition of ultrasound to mammogram could replace MRI, where MRI is not available or not feasible for the patient (e.g., claustrophobia, pacemakers, electronic/magnetic/mechanical implants, magnetic clips, etc.); however, MRI has higher sensitivity for breast screening.
    - In women 70 years and older, the decision to continue mammography should depend on life expectancy and preference.
    - Clinical breast exam should be offered at 6-month intervals starting at age 25 years.
    - Pregnant and lactating women should be offered clinical breast exam every 6 months. Mammography and MRI can resume post partum.
    - Male *BRCA1* and *BRCA2* mutation carriers should be offered a clinical breast exam every 12 months. Surveillance imaging studies are not recommended.
    - Individuals who wish to pursue breast self-examination, should be counseled about the potential benefits and limitations, and should be offered information on technique.
3. Other Risk Reduction Strategies
    - Chemoprevention: The potential benefit and risks associated with preventive tamoxifen can be discussed. This discussion should be led by a physician who is well-informed on the potential benefits and risks associated with tamoxifen. Of note, tamoxifen has only been found to reduce the risk of hormone sensitive cancers. As 80% of *BRCA1* cancers are estrogen receptor negative, the expected benefit would be less for this population.
    - Bilateral oophorectomy: The benefit (e.g., 53%-68% risk reduction) of prophylactic bilateral oophorectomy on breast cancer risk if performed in the premenopausal period should be raised for *BRCA1* and *BRCA2* mutation carriers but can also be discussed on a case-by-case basis for other women in the target population. The full recommendation on prophylactic bilateral oophorectomy follows in the next section (*Ovarian Cancer Risk Reduction and Surveillance*).

Ovarian Cancer Risk Reduction and Surveillance

1. Surgery: Prophylactic Bilateral Salpingo-Oophorectomy
    - The benefits and risks of prophylactic bilateral salpingo-oophorectomy plus/minus hysterectomy should be raised for *BRCA1* and *BRCA2* mutation carriers but can also be discussed on a case-by-case basis for other women in the target population.
        - The issue of premature menopause and the possibility of an incidental ovarian or fallopian tube cancer being diagnosed should be discussed in advance.
        - Prophylactic bilateral salpingo-oophorectomy plus/minus hysterectomy should be performed by a gynecologist. Laparoscopy should be undertaken if possible. Surgery should be directed towards complete removal of both ovaries and fallopian tubes. Peritoneal surfaces should be inspected and fluid collected for cytological analysis.
        - Excised tissue should be examined by a pathologist who is aware of the individual's high genetic risk status and who is experienced in ovarian cancer pathology. A protocol for the pathological evaluation of tissue specimens can be found in the appendix of the original guideline document.
        - In most instances, this procedure can be delayed until age 35-40 years.
    - Hormone replacement therapy can be considered in premenopausal women undergoing prophylactic oophorectomy.
        - It should be used for as short a duration as possible and not beyond the average age for natural menopause.
        - Estrogen only is preferred but should only be prescribed in the setting of hysterectomy. A gynecologist should be available for consultation.
        - If an individual has had a prior breast cancer diagnosis, hormone replacement therapy is generally not recommended, and should not be considered without assessment by a multidisciplinary team.
2. Other Risk Reduction Strategies
    - Oral contraceptives: Premenopausal individuals currently using, or contemplating the use of, oral contraceptive pills should be counseled on the probable protective effect against ovarian cancer but uncertainty surrounding increased breast cancer risk. Oral contraceptive pills should not be prescribed solely for the purpose of ovarian cancer risk reduction.
    - Ovarian cancer surveillance: screening for ovarian cancer is controversial and generally not recommended. Individuals should be counseled on the limitations of the currently available surveillance methods and the symptoms/signs of ovarian cancer. A gynecologist with expertise in the high-risk field should be available for consultation.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Breast and ovarian cancer

Guideline Category

Counseling

Management

Risk Assessment

Screening

Clinical Specialty

Family Practice

Internal Medicine

Medical Genetics

Obstetrics and Gynecology

Oncology

Pathology

Psychology

Radiology

Surgery

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Nurses

Physician Assistants

Physicians

Psychologists/Non-physician Behavioral Health Clinicians

Guideline Objective(s)

To develop consensus-based recommendations on risk reduction and surveillance strategies for individuals at high genetic risk for breast and ovarian cancer

Target Population

Individuals who meet one of the following criteria:

- Are found to carry a deleterious mutation in *BRCA1* or *BRCA2*
- Have not undergone genetic testing but have a first degree relative with a deleterious mutation in *BRCA1* or *BRCA2*
- Are assessed to be at high risk for hereditary breast/ovarian cancer as per a formal consultation with a medical geneticist or after assessment at a high risk clinic (i.e., an individual with a projected lifetime breast cancer risk of at least 20%–25% based on family history models)

Interventions and Practices Considered

1. Bilateral mastectomy in women who are *BRCA1* and *BRCA2* mutation carriers
2. Mammography and magnetic resonance imaging (MRI) screening on an annual basis for women with intact breasts
3. Clinical breast examination
4. Breast self-examination
5. Counseling on benefits, risks, and limitations of all risk reduction and surveillance strategies
6. Chemoprevention with tamoxifen
7. Bilateral oophorectomy
8. Bilateral salpingo-oophorectomy plus/minus hysterectomy
9. Examination of excised tissue by a trained pathologist
10. Hormone replacement therapy in premenopausal women undergoing prophylactic oophorectomy
11. Counseling on oral contraceptive use
12. Screening for ovarian cancer (generally not recommended)

Major Outcomes Considered

- Risk of breast or ovarian cancer
- Sensitivity, specificity, and diagnostic odds ratio of surveillance strategies
- Breast or ovarian cancer-specific mortality

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Research Questions

Specific research questions to be addressed by the guideline document were formulated by the guideline lead(s) and Knowledge Management (KM) Specialist using the PICO question format (patient or population, intervention, comparisons, outcomes).

Guideline Question

What breast and ovarian cancer risk reduction and surveillance options should be offered to individuals with high genetic risk?

Search Strategy

The original guideline was developed using evidence from existing guidelines, which was gathered by searching PubMed and clinical practice guideline organizations' websites (e.g., the National Comprehensive Cancer Network [NCCN], Cancer Care Ontario [CCO], National Institute for Health and Clinical Excellence [NICE], etc.) for relevant practice guidelines. Practice guidelines were considered if they met the following criteria: (1) published, updated, or available in draft form (in the English language) from January 2006 through February 2007; (2) pertained to the care of individuals with high genetic risk for breast plus/minus ovarian cancer; (3) had recommendations with clear links to the supporting literature; and (4) had notation of where expert opinion was employed. Specific guidelines pertaining to the use of breast screening with magnetic resonance imaging (MRI) were also sought.

The most relevant comprehensive guidelines selected for full review were from the National Hereditary Cancer Task Group (NHCTF), NICE, and NCCN. The most relevant specific guidelines pertaining to the use of breast screening with MRI were from CCO and the American Cancer Society (ACS).

The guideline was updated using evidence identified by searching the Ovid Medline, EMBASE, Cochrane Database of Systematic Reviews, National Guideline Clearinghouse, and relevant conference websites (all 2007 through September 27, 2010) for new or recently updated clinical practice guidelines, systematic reviews, clinical trials, abstracts, and other relevant evidence deemed eligible to inform the topic. Reference lists of related papers and recent review articles were also scanned for additional citations. Search terms included 'hereditary breast and ovarian cancer' or 'breast and ovarian cancer syndrome' with a limit of English language.

Number of Source Documents

The current search identified a total of 41 citations: seven new or updated guidelines, four systematic reviews, two meta-analyses, and 28 original articles.

Methods Used to Assess the Quality and Strength of the Evidence

Not stated

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Evidence was selected and reviewed by a working group comprised of members from the Alberta Provincial Breast Tumour Team and Knowledge Management (KM) Specialist from the Guideline Utilization Resource Unit (GURU). A detailed description of the methodology followed during the guideline development process can be found in the Guideline Utilization Resource Unit Handbook (see the "Availability of Companion Documents" field).

Evidence Tables

Evidence tables containing the first author, year of publication, patient group/stage of disease, methodology, and main outcomes of interest are assembled using the studies identified in the literature search. Existing guidelines on the topic were assessed by the KM Specialist using portions of the Appraisal of Guidelines Research and Evaluation (AGREE) II instrument (http://www.agreetrust.org) and those meeting the minimum requirements were included in the evidence document. Due to limited resources, GURU does not regularly employ the use of multiple reviewers to rank the level of evidence; rather, the methodology portion of the evidence table contains the pertinent information required

for the reader to judge for himself the quality of the studies.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Formulating Recommendations

The working group members formulated the guideline recommendations based on the evidence synthesized by the Knowledge Management Specialist during the planning process, blended with expert clinical interpretation of the evidence. As detailed in the Guideline Utilization Resource Unit Handbook (see the "Availability of Companion Documents" field), the working group members may decide to adopt the recommendations of another institution without any revisions, adapt the recommendations of another institution or institutions to better reflect local practices, or develop their own set of recommendations by adapting some, but not all, recommendations from different guidelines.

The degree to which a recommendation is based on expert opinion of the working group and/or the Provincial Tumour Team members is explicitly stated in the guideline recommendations. Similar to the American Society of Clinical Oncology (ASCO) methodology for formulating guideline recommendations, Guideline Utilization Resource Unit does not use formal rating schemes for describing the strength of the recommendations, but rather describes, in conventional and explicit language, the type and quality of the research and existing guidelines that were taken into consideration when formulating the recommendations.

A multidisciplinary panel from the Alberta Health Services, Calgary High Risk Breast and Ovarian Cancer Interest Group was convened in early 2007 to undertake a guideline adaptation process. The panel included representation from medical genetics (medical geneticist and counselors), breast surgery, gynecology, radiology, medical oncology, psychology, and nursing.

Panel members first met March 21, 2007. The selected guidelines were reviewed and recommendations were adopted or adapted for local use. Consensus was defined as two-thirds quorum but minority opinions and reasons were recorded, as necessary. The adapted guideline was written by the panel chair and reviewed by all panel members. The guideline was updated using evidence identified by literature search.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

This guideline was reviewed and endorsed by the Alberta Provincial Breast Tumour Team and academic Medical Genetics Departments affiliated with the University of Calgary and the University of Alberta.

When the draft guideline document is completed, revised, and reviewed by the Knowledge Management Specialist and the working group members, it is sent to all members of the Provincial Tumour Team for review and comment. The working group members then make final revisions to the document based on the received feedback, as appropriate. Once the guideline is finalized, it is officially endorsed by the Provincial Tumour Team Lead and the Executive Director of Provincial Tumour Programs.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate use of risk reduction and surveillance strategies for individuals at high genetic risk for breast and ovarian cancer

Potential Harms

- Preservation of the nipple and areola could be considered with prophylactic bilateral mastectomy; however the patient should be informed that there is currently little evidence on this topic and that there may be a slightly increased risk of breast cancer (versus complete removal of nipple and areola) and possible loss of sensation and ischemia.
- Individuals should be informed of the potential for false negative results (leading to a breast cancer diagnosis between screening rounds) and false positive results (leading to recall imaging studies and possibly unnecessary biopsies) associated with mammography and magnetic resonance imaging (MRI) for breast cancer screening.

Contraindications

Contraindications

- Tamoxifen is contraindicated during pregnancy and should be delayed until child-bearing is complete in the setting of risk reduction.
- Mammography and magnetic resonance imaging (MRI) should not be used for surveillance during pregnancy or lactation.

Qualifying Statements

Qualifying Statements

The recommendations contained in this guideline are a consensus of the Alberta Provincial Breast Tumour Team and represent a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

Implementation of the Guideline

Description of Implementation Strategy

- Present the guideline at the local and provincial tumour team meetings and weekly rounds.
- Post the guideline on the Alberta Health Services Web site.
- Send electronic notification of guideline updates to members of Alberta Health Services Cancer Care.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2011 Apr

Guideline Developer(s)

CancerControl Alberta - State/Local Government Agency [Non-U.S.]

Source(s) of Funding

Alberta Health Services, Cancer Care

Guideline Committee

Alberta Provincial Breast Tumour Team

Composition of Group That Authored the Guideline

Not stated

Financial Disclosures/Conflicts of Interest

All panel members were asked to disclose information on potential conflicts of interest prior to initiation of the first meeting (none disclosed).

Participation of members of the Alberta Provincial Breast Tumour Team in the development of this guideline has been voluntary and the authors have not been remunerated for their contributions. There was no direct industry involvement in the development or dissemination of this guideline. Alberta Health Services, Cancer Care recognizes that although industry support of research, education and other areas is necessary in order to advance patient care, such support may lead to potential conflicts of interest. Some members of the Alberta Provincial Breast Tumour Team are involved in research funded by industry or have other such potential conflicts of interest. However the developers of this guideline are satisfied it was developed in an unbiased manner.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the Alberta Health Services Web site .

Availability of Companion Documents

The following is available:

- Guideline utilization resource unit handbook. Edmonton (Alberta): Alberta Health Services, Cancer Care; 2011 Dec. 5 p. Electronic copies: Available in Portable Document Format (PDF) from the Alberta Health Services Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on December 20, 2012. The information was verified by the guideline developer on February 5, 2013.

Copyright Statement

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